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(54) Fast dissolving tablet and its production

Schnelllösliche Tablette und ihre Herstellung

Comprimé à dissolution rapide et sa fabrication

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(73) Proprietor: **TAKEDA CHEMICAL INDUSTRIES,
LTD.**
Chuo-ku, Osaka 541 (JP)

(72) Inventors:
• **Makino, Tadashi**
Ibaraki, Osaka 567 (JP)
• **Yamada, Masayuki**
Kawanishi, Hyogo 666-01 (JP)

• **Kikuta, Jun-ichi**
Suita, Osaka 565 (JP)

(74) Representative:
von Kreisler, Alek, Dipl.-Chem. et al
Patentanwälte
von Kreisler-Selting-Werner
Postfach 10 22 41
50462 Köln (DE)

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Description**FIELD OF THE INVENTION**

5 **[0001]** The present invention relates to a fast dissolving tablet comprising a pharmacologically active ingredient, such as a vitamin, antipyretic-analgesic-antiinflammatory agent, antihypertensive drug, psychotropic drug or antidiabetic drug and a carbohydrate, having an adequate strength and capable of dissolving and disintegrating at a high rate in the oral cavity and to a method of producing the tablet.

BACKGROUND OF THE INVENTION

15 **[0002]** Recently much research has been undertaken in the geriatric field ranging from the physiology of aging to the design of drugs and pharmaceutical preparations to daily care and assistance. According to, inter alia, the silver science research conducted by the Ministry of Health and Welfare, there is an interesting research report entitled 'Studies for the construction of new pharmaceutical preparations and new packaging containers optimal for administration to elderly subjects' (Masayasu Sugihara, Tokyo Women's Medical College, and others) (August 22, 1989 issue of the Yakuji Nippo). By way of illustration, as such new preparations, a) buccal dissolution type preparations, b) paste-like preparations and c) jelly-like preparations are described. Particularly buccal dissolution type and paste-like preparations are claimed to be easy for elderly persons to ingest and excellent in stability. The buccal dissolution type preparations, in particular, contain polyethylene glycol 1000 as the base which dissolves in the oral cavity and an oleaginous base as the base which melts at the temperature prevailing in the oral cavity and, in consideration of sensory factors such as taste and texture as well as moldability, further contain sucrose and mannitol. These are molded by filling the pocket of a vinyl chloride molding sheet for press-through package (PTP) use with a heat-melted medicated base and allowing it to cool and take form. In this manner, a buccal dissolution type solid preparation for elderly persons is manufactured.

25 **[0003]** Japanese Patent Laid-open No. 76420/1977 describes a method of manufacturing a porous tablet which features a high disintegration rate insuring rapid dissolution in the oral cavity which comprises placing a magmatic mixture or solution containing 5 to 80% by weight of an inert solvent freezing at a temperature of -30°C to 25°C and the balance of a tablet-forming composition in an inert cooling medium such as liquid nitrogen to cause solidification, then compressing the resulting granules into tablets at a temperature not higher than the freezing point of the solvent, and finally removing the solvent by freeze-drying or air drying.

30 **[0004]** Japanese Patent Publication No. 24410/1983 discloses a method of manufacturing a porous tablet with good disintegrability which comprises mixing a tablet-constituting composition with a solvent which is inert to said composition and freezes at a temperature of -30 to +25°C (for example, water, cyclohexane or benzene), the proportion of said solvent being 5 to 80% by weight, placing the resulting mixture in an inert cooling medium for solidification, compressing the resulting solid into tablets at a temperature lower than the freezing point of said solvent and evaporating the solvent by freeze-drying or spontaneous drying.

35 **[0005]** Japanese Patent Laid-open No. 15830/1986 discloses an antacid composition having a porous and extra fine crystal structure which comprises an antacid and a base for confectionery comprising a sweetener for confectionery and a plasticizer.

40 **[0006]** On the other hand, in foreign countries, there are guidelines (e.g. USA "FDA 1983) for research concerning pharmaceutical products for elderly persons and, as a buccal dissolution type solid preparation, Zydys from R.P. Scherer, England, is commercially available, for instance. While the composition of this preparation is not known, it is manufactured by blending an active ingredient with a polymer, sugar and other ingredients, dissolving the blend and freeze-drying the solution (Manuf. Chemist. Feb. 36, 1990).

45 **[0007]** However, from the standpoint of practical utility as buccal preparations, the conventional products described above are not fully satisfactory in shelf-life, solubility and the scope of compatible medicament. For Example, the composition described in said Japanese Patent Laid-open No. 15830/1986 is prepared by heating and melting the ingredients, so that it is inferior in the scope of compatible medicament and disintegrability of the preparation in the oral cavity. Also, Zydys (trade name) mentioned above has problems with the water solubility of the active ingredient, mechanical strength of the preparation, and % content of the active ingredient so that it is not satisfactory, either, for administration to patients of advanced age.

50 **[0008]** Furthermore, a tablet which disintegrates and dissolves quickly is generally weak in mechanical strength. Therefore, it has been considered necessary to develop a preparation which offers practically acceptable disintegration and dissolution speeds in the oral cavity and, at the same time, possesses a sufficient mechanical strength so that it will not be destroyed in the course of manufacture and subsequent distribution.

SUMMARY OF THE INVENTION

[0009] It is an object of the present invention to provide a fast dissolving tablet having adequate disintegrability and solubility in the oral cavity and sufficient mechanical strength to resist destruction in the course of manufacture and storage.

[0010] It is another object of the invention to provide a method of producing a fast dissolving tablet, by which a tablet having the above-mentioned desirable properties can be produced without requiring complicated production procedures.

[0011] It is a further object of the invention to provide a fast dissolving tablet which is easy for elderly persons and children to ingest and is, therefore, practically useful and a method of producing the tablet.

[0012] Under the circumstances described above, the inventors of the present invention found, after much research for designing a buccal dissolution type pharmaceutical preparation, that when a mixture comprising a pharmacologically active ingredient, a specific carbohydrate component and a barely sufficient amount of water to moisten the surface of particles of the carbohydrate component is compression-molded and afterwards dried, there is surprisingly obtained a porous tablet having sufficient mechanical strength resisting destruction in the course of manufacture, storage and distribution and yet capable of disintegrating and dissolving rapidly in the oral cavity without resort to complex production steps which are usually required, such as heating, melting, dissolving, freezing, and that this tablet is fully suitable for use as a buccal dissolution type tablet. The present invention has been brought into being on the basis of the above findings.

[0013] The present invention thus provides

(1) a fast dissolving or disintegrating tablet which comprises an effective amount of an active ingredient and a carbohydrate component, wherein said carbohydrate component comprises at least erythritol, and which has a porous structure with a hardness of 2 to 25 kg as determined with the tablet hardness tester TH-100 from Toyama Sangyo and a porosity of 20 to 80% as determined according to the following equation:

$$\text{Porosity} = \frac{\text{Vol. of tablet} - (\text{wt. of tablet} / \text{true density of ingredients})}{\text{Vol. of tablet}} \times 100;$$

(2) a fast dissolving or disintegrating tablet obtainable by a method which comprises

(a) wetting a mixture comprising an active ingredient and a carbohydrate component with 0.3 to 10% by weight of water, based on the weight of a composition comprising said active ingredient, said carbohydrate and water, to moisten the surface of particles of said carbohydrate component, wherein said carbohydrate component comprises at least erythritol;

(b) compression molding said composition into a fast dissolving or disintegrating tablet form; and
(c) drying said tablet; and

(3) the use of erythritol for producing a fast dissolving or disintegrating tablet comprising an active ingredient and erythritol as a carbohydrate component.

[0014] The fast dissolving tablet of the present invention as defined in (1) and (2) above can be manufactured by compression-molding a composition comprising a pharmacologically active ingredient, the carbohydrate component and a barely sufficient amount of water to wet the surface of particles of the carbohydrate component into a tablet form.

[0015] Said fast dissolving tablet can be suitably utilized as a buccal dissoluble and disintegratable tablet because of its easy solubility and disintegrability in the oral cavity.

[0016] As the pharmacologically active ingredient, there may be mentioned vitamins, crude drugs, antipyretic-analgesic-antiinflammatory agents, antianxiety drugs, hypnotic-sedative agents, gastrointestinal function conditioning agents, antitussive-expectorants, antihypertensive drugs, antidiabetic agents, drugs for osteoporosis and skeletal muscle relaxants. The proper proportion of the pharmacologically active ingredient in said composition is 0.05 to 90% by weight.

The carbohydrate component which can be used comprises at least erythritol and may further include sucrose, starch sugars, sugar alcohols and other tetroses.

[0017] The carbohydrate content of said composition may, for example, range from 10 to 90% by weight.

[0018] The pressure for compression-molding may, for example, range from 3 to 160 kg/cm².

[0019] The fast dissolving tablet of the present invention has a porous structure with a porosity of 20 to 80%.

DETAILED DESCRIPTION OF THE INVENTION

[0020] The pharmacologically active ingredient for use in the present invention may be in any optional form, for example, a solid, particulate, granular, crystalline, or oily or solution form. The active ingredient may be at least one member selected from the group consisting of nourishing and health-promoting agents, antipyretic-analgesic-inflammatory agents, antipsychotic drugs, antianxiety drugs, antidepressants, hypnotic-sedative agents, spasmolytics, gastrointestinal function conditioning agents, antacids, antitussive-expectorants, dental buccal drugs, antihistamines, cardiotonics, antiarrhythmic drugs, diuretics, antihypertensive drugs, vasoconstrictors, coronary vasodilators, peripheral vasodilators, cholagogues, antibiotics, chemotherapeutic drugs, antidiabetic agents, drugs for osteoporosis and skeletal muscle relaxants.

[0021] Among said nourishing and health-promoting agents are various vitamins such as vitamin A, vitamin D, vitamin E (d- α -tocopherol acetate), vitamin B₁ (dibenzoylthiamin, fursultiamine hydrochloride), vitamin B₂ (riboflavin butyrate), vitamin B₆ (pyridoxine hydrochloride), vitamin C (ascorbic acid, sodium L-ascorbate), vitamin B₁₂ (hydroxocobalamin acetate); minerals such as calcium, magnesium, iron; proteins; amino acids; oligosaccharides and crude drugs.

[0022] Among said antipyretic-analgesic-antiinflammatory agents are aspirin, acetaminophen, ethenzamide, ibuprofen, diphenhydramine hydrochloride, dl-chlorpheniramine maleate, dihydrocodeine phosphate, noscapine, methyl-ephedrine hydrochloride, phenylpropanolamine hydrochloride, caffeine, serratiopeptidase, lysozyme chloride, tofenamic acid, mefenamic acid, diclofenac sodium, flufenamic acid, salicylamide, aminopyrine, ketoprofen, indomethacin, bucolome, pentazocine.

[0023] Among said antipsychotic drugs are chlorpromazine, reserpine. The antianxiety drugs include chlordiazepoxide, diazepam. The antidepressants include imipramine, maprotiline, amphetamine.

[0024] Among said hypnotic-sedatives are estazolam, nitrazepam, diazepam, phenobarbital sodium. The spasmolytics include scopolamine hydrobromide, diphenhydramine hydrochloride, papaverine hydrochloride.

[0025] The gastrointestinal function conditioning agents include stomachic-digestives such as diastase, saccharated pepsin, scopolia extract, lipase AP, cinnamon oil, and intestinal function controlling drugs such as berberine chloride, resistant lactic acid bacterium, Lactobacillus bifidus. As said antacids, there may be mentioned magnesium carbonate, sodium hydrogen carbonate, magnesium aluminometasilicate, synthetic hydrotalcite, precipitated calcium carbonate, magnesium oxide.

[0026] The antitussive-expectorants include cloperastine hydrochloride, dextromethorphan hydrobromide, theophylline, potassium guaiacolsulfonate, gnaifenesis.

[0027] The dental buccal drugs include oxytetracycline, triamcinolone acetonide, chlorhexidine hydrochloride, lidocaine.

[0028] The antihistamines include diphenhydramine hydrochloride, promethazine, isothipendyl hydrochloride, dl-chlorpheniramine maleate.

[0029] The cardiotonics include etilefrine hydrochloride and so on. The antiarrhythmic drugs include procainamide hydrochloride, propranolol hydrochloride, pindolol.

[0030] The diuretics include isosorbide, furosemide.

[0031] The antihypertensive drugs include delapril hydrochloride, captopril, hexamethonium bromide, hydralazine hydrochloride, labetalol hydrochloride, methyl dopa.

[0032] The vasoconstrictors include phenylephrine hydrochloride. The coronary vasodilators include carbocromen hydrochloride, molsidomine, verapamil hydrochloride. The peripheral vasodilators include cinnarizine. The cholagogues include dehydrocholic acid, trepibutone.

[0033] The antibiotics include cepheems, penems and carbapenems such as cefalexin, amoxicillin, pivmecillinam hydrochloride, cefotiam dihydrochloride. The chemotherapeutic drugs include sulfamethizole, thiazosulfone. The antidiabetic agents include tolbutamide, voglibose. The drugs for osteoporosis include ipriflavone. The skeletal muscle relaxants include methocarbamol.

[0034] The active ingredient may have been diluted with a diluent which is used generally in the pharmaceutical or food industry. At least one of active ingredients may be oily.

[0035] Preferred examples of such active ingredient for purposes of the present invention are the vitamins, crude drugs, antipyretic-analgesic-antiinflammatory agents, antianxiety drugs, hypnotic-sedative agents, gastrointestinal function conditioning agents, antitussive-expectorants, antihypertensive drugs, antidiabetic agents, drugs for osteoporosis, skeletal muscle relaxants mentioned hereinbefore.

[0036] The recommendable proportion of the active ingredient in the composition comprising it, a carbohydrate component and water is dependent on its type but is generally 0.05 to 90% by weight and preferably 0.1 to 70% by weight and more preferably 0.3 to 60 % by weight. The carbohydrate component for use in the present invention comprises at least erythritol and may further comprise other carbohydrates that are soluble in water and do not adversely affect the active ingredient (for example, decomposition of the active ingredient). Thus, for example, sugar, starch sugars, lactose, honey, sugar alcohols and other tetroses can be employed.

[0037] The sugar includes, among others, sucrose, coupling sugar, fructoligosaccharides, palatinose.

The starch sugars include, among others, glucose, maltose, powdered syrup, starch syrup, isomerized sugar (fructose). The lactose includes, among others, lactose, isomerized lactose (lactulose), reduced lactose (lactitol). The honey may be any of the various types which are commonly used as food. The sugar alcohol includes, among others, sorbitol, mannitol, reduced malt syrup (maltitol), reduced starch saccharides, xylitol, reduced palatinose.

Tetroses obtainable by fermentation of glucose can also be employed. These carbohydrates can be used independently or in combination.

[0038] Mean particle size of the carbohydrate component is usually in the range of 1 to 100 μm , preferably 20 to 70 μm and more preferably 30 to 50 μm .

[0039] The proportion of the carbohydrate component in the above composition varies with the type of active ingredient but generally speaking may be about 10 to 90% by weight, preferably about 20 to 85% by weight and, for still better results, about 30 to 80% by weight.

[0040] In the case where the proportion of the active ingredient is in the range of 0.1 to 10 % by weight in the composition, where the dosage of the active ingredient is little, the proportion of the carbohydrate component in the composition is generally in the range of 30 to 90 % by weight, preferably 50 to 85 % by weight and more preferably 60 to 85 % by weight. As the examples of the active ingredient whose dosage is little, there may be mentioned diazepam.

[0041] In the case where the proportion of the active ingredient is in the range of 10 to 30 % by weight in the composition, where the dosage of the active ingredient is moderate, the proportion of the carbohydrate component in the composition is generally 20 to 90 % by weight, preferably 30 to 80 % by weight and more preferably 40 to 75 % by weight. As the examples of the active ingredient whose dosage is moderate, there may be mentioned antipyretic-analgesic-inflammatory agents.

[0042] In the case where the proportion of the active ingredient is in the range of 30 to 70 % by weight in the composition, where the dosage of the active ingredient is much, the proportion of the carbohydrate component in the composition is usually 10 to 70 % by weight, preferably 15 to 60 % by weight and more preferably 20 to 50 % by weight. As the examples of the active ingredient whose dosage is much, there may be mentioned vitamin C.

[0043] Unless the object of the invention is interfered with, the above-mentioned composition may further contain a variety of additives which are commonly employed in the manufacture of tablets.

[0044] The additives mentioned above include, among others, disintegrators, binders, acids, foaming agents, artificial sweeteners, flavorants, lubricants, colorants.

[0045] The disintegrators include, among others, corn starch, potato and other starches, carmellose calcium, carmellose sodium and polyvinyl alcohol. The binders include, among others, gum arabic powder, gelatin and pullulan.

[0046] The acids include citric acid, tartaric acid and malic acid. The foaming agents include sodium hydrogen carbonate. The artificial sweeteners include saccharin sodium, dipotassium glycyrrhizinate, aspartame, stevia, thaumatin

[0047] The flavorants include lemon, lime, orange and menthol. The lubricants include, among others, magnesium stearate, sucrose fatty acid ester, polyethylene glycols, talc and stearic acid. The colorants include, among others, various food colors such as FD&C Yellow No. 6, FD&C Red No. 2, FD&C Blue No. 2, food lakes, red iron oxide.

[0048] One or more of these additives can be added in appropriate proportions, for example at the blending of the active ingredient with the carbohydrate, at addition of water, in the course of kneading or before and after any of such stages.

[0049] The amount of water in said composition may be a barely sufficient amount to moisten the surface of particles of said carbohydrate component. In the present invention, the surface of particles of the carbohydrate component is wetted, so that particles of the carbohydrate component adhere to each other mainly at the surface of said particles to give a porous tablet having adequate porosity and hardness to buccal tablet by compression-molding.

[0050] The proper amount of water, which depends on the types and amounts of active ingredient, carbohydrate component and additives, may be generally 0.3 to 10% by weight, preferably 0.3 to 7% by weight, more preferably 0.5 to 3% by weight, for still better results, about 0.7 to 3% by weight and most preferably 1 to 3% by weight based on the weight of the above composition. If the amount of water is too small, the mechanical (falling impact) strength of tablets will not be sufficiently high, while the use of an excessive amount of water tends to cause adhesion of the active ingredient and others to the molding equipment (for example, the punch and die cavity), thus interfering with molding. To be specific, when the composition contains 55 to 75% by weight of erythritol water is generally added in a proportion of 1.5 to 2.5% by weight.

[0051] The amount of water may be controlled by adding water to an optional ingredient or mixture thereof, and addition method of water is not limited, and water may be added at once or drop by drop or being sprayed.

[0052] For example, to a blended mixture of the active ingredient with the carbohydrate and, if necessary, said additives may be added a barely sufficient amount of water to moisten the surface of carbohydrate particles in said mixture.

[0053] The blending of the above ingredients can be carried out by any of the conventional blending techniques such as mixing, kneading, sieving, Specifically, Vertical Granulator GV10 (Powrex), Universal Kneader (Hata Iron Works, Ltd.), fluidized bed granulator FD-5S (Powrex) and Gyrosifter (Tokuju Seisakusho) can be employed.

[0054] The composition comprising an active ingredient, a carbohydrate component and water is usually kneaded before making tablets.

[0055] The kneading operation of the composition containing water can be carried out by the routine method commonly used in the art. For example, the devices mentioned hereinbefore for the blending of the ingredients can be utilized.

[0056] The molding of tablets can be carried out using the equipment commonly used in the granulation and compression-molding of tablets. For example, a single-punch tablet machine (Kikusui Seisakusho) or a rotary tablet machine (Kikusui Seisakusho) can be employed. The molding pressure is generally 3 to 160 kg/cm², preferably 5 to 130 kg/cm² and for still better results, 8 to 50 kg/cm². The molding temperature is such a temperature that particles of the carbohydrate are not dissolved nor melted, and is generally ambient temperature (20 to 30°C) and preferably 25°C.

[0057] The tablets thus molded are preferably dried. The drying operation can be carried out by any of the techniques used commonly in the art, such as vacuum drying, freeze drying, spontaneous drying.

[0058] These tablets can be coated to the extent not adversely affecting the hardness or solubility of the tablets by any coating method that is generally used in the manufacture of coated tablets.

[0059] The fast dissolving tablet thus obtained has a porous structure. The term 'porous structure' is used herein to mean a tablet having a porosity of generally 20 to 80% and preferably 30 to 70%. This porous tablet is excellent in disintegrability and solubility in the oral cavity and has a high falling impact strength.

[0060] Thus, the tablet of the invention has a buccal solubility (a time to complete dissolution by saliva in the oral cavity in a healthy adult male) of generally 0.05 to 3.0 minutes and preferably 0.1 to 1.5 minutes, a disintegration time (a time measured by the disintegration test described in Japanese Pharmacopoeia XII) of generally 0.05 to 3.0 minutes and preferably 0.1 to 1.5 minutes, a hardness (a value measured with tablet hardness tester) of generally 2 to 25 kg and preferably 3 to 20 kg, and a falling impact strength (a degree of destruction when the tablet is dropped from a height of 30 cm on a glass plate) of generally 0 to 70% and preferably 0 to 40%.

[0061] Therefore, the fast dissolving tablet of the present invention can be used for the therapy or prophylaxis of various diseases just as the conventional preparations containing the same active ingredient but with an increased ease of ingestion by elderly persons and children and also as safe preparations for general adults. The tablet of the invention further features a long shelf-life.

[0062] The fast dissolving tablet of the present invention contains the active ingredient in a proportion of generally 0.05 to 90% by weight, preferably 0.1 to 70% by weight, more preferably 0.3 to 60% by weight and the carbohydrate component in a proportion of generally 10 to 90% by weight, preferably 20 to 85% by weight and, for still better results, 30 to 80% by weight.

[0063] In the case where the dosage of the active ingredient is little, the tablet of the invention contains the active ingredient in a proportion of generally 0.1 to 10% by weight, and the carbohydrate component in a proportion of generally 30 to 90% by weight, preferably 50 to 85% by weight and more preferably 60 to 85% by weight.

[0064] In the case where the dosage of the active ingredient is moderate, the tablet of the invention contains the active ingredient in a proportion of generally 10 to 30% by weight, and the carbohydrate component in a proportion of generally 20 to 90% by weight, preferably 30 to 80% by weight and more preferably 40 to 75% by weight.

[0065] In the case where the dosage of the active ingredient is much, the tablet of the invention contains the active ingredient in a proportion of generally 30 to 70% by weight, and the carbohydrate component in a proportion of generally 10 to 70% by weight, preferably 15 to 60% by weight and more preferably 20 to 50% by weight.

[0066] The fast dissolving tablet of the invention can be dosed just as the conventional oral preparations containing the same active ingredient. The dosage of the tablet of the invention varies according to the type of active ingredient and the patient's age, sex and condition, among other factors. For example, in the case where the active ingredient is diazepam, the tablet is generally administered for adults such that a daily dosage of the active ingredient is in the range of 0.01 to 100 mg, preferably 0.1 to 30 mg, and for still better results, 0.3 to 10 mg once a day or in 2 or 3 divided doses. Also, when the vitamin C-containing tablet of the invention is administered as a nourishing and health promoting drug, the dosage of the tablet is 2 to 2000 mg/day and preferably 100 to 2000 mg/day as vitamin C.

[0067] The fast dissolving tablet of the invention is easy to ingest because it is readily disintegratable and soluble in the oral cavity and has a long shelf life because it has an adequate mechanical strength. Therefore, the tablet can be advantageously used for the prevention or treatment of diseases in patients, particularly aged and pediatric patients.

[0068] In accordance with the manufacturing method of the invention, the easily disintegratable troche having the above-mentioned excellent characteristics can be easily manufactured without resort to complicated procedures.

[0069] The following examples further illustrate the present invention. The following Examples 1, 2, 4-11 and 13-24 and Reference Examples 1, 2 and 4 do not form part of the invention but represent background art useful for understanding the invention.

EXAMPLES

Reference Example 1

[0070] A granulating machine (Vertical Granulator VG10, Powrex) was charged with ascorbic acid, riboflavin butyrate, d- α -tocopherol, xylitol, maltitol, corn starch, aspartame and powdered acacia in the amounts indicated in Table 1 and the charge was stirred for 1 minute. Then, 200 ml of water was added and the mixture was kneaded. The kneaded mass was dried in vacuo using a box type vacuum dryer (Kusuki Seisakusho) and comminuted with a sifting granulator (Powermill, Showa Chemical Machinery). After addition of magnesium stearate (0.5%), the granules were blended in a tumbler mixer (Showa Chemical Machinery) for 3 minutes. Using a single-punch tablet machine (Kikusui Seisakusho), the above granules were compression-molded with a flat punch having a beveled edge, 20 mm in diameter, at a molding pressure of 1910 bar (kg/cm²) (force: 6000 kg) to provide about 900 tablets.

Reference Example 2

[0071] A kneader (Universal Blender, Hata Iron Works) was charged with diazepam, sucrose, glucose, potato starch, citric acid, gelatin and FD&C Yellow No. 6 in the amounts indicated in Table 2 and the charge was blended for 2 minutes. Then, 50 ml of alcohol and 50 ml of water were added and the mixture was kneaded. The kneaded mass was dried in vacuo using a box type vacuum dryer (Kusuki Seisakusho) and comminuted with a cutter mill (Fitzmill, Hosokawa Micron). After Addition of sucrose fatty acid ester (0.5%), the granules were mixed with a mixer (V Mixer, Patterson-Kelly) for 1 minute. Then, using a rotary tablet machine (Correct 19K, Kikusui Seisakusho), the granules were compression-molded with a flat punch having a beveled edge, 15 mm in diameter, at a molding pressure of 1980 bar (kg/cm²) (force: 3500 kg) to provide about 900 tablets.

Reference Example 3 (not encompassed by the tablets according to claims 1 to 20)

[0072] A fluidized-bed granulator (FD-5S, Powrex) was charged with ibuprofen, caffeine, erythritol, citric acid, carmellose calcium, corn starch, stevia and menthol in the amounts indicated in Table 3 and the charge was mixed for 3 minutes. Then, 120 ml of water was sprayed and the mixture was further granulated. The granules were dried and comminuted with a cutter mill (Power Mill, Showa Chemical Machinery). To the granules were added 0.2% of magnesium stearate and 1.8% of talc and the mixture was blended with a mixer (Tumbler Mixer, Showa Chemical Machinery) for 3 minutes. Then, the granules were compression-molded with a rotary tablet machine (Correct 19K, Kikusui Seisakusho) with a flat punch having a beveled edge, 15 mm in diameter, at a molding pressure of 1700 bar (kg/cm²) (force: 3000 kg) to provide about 900 tablets.

Reference Example 4

[0073] The procedure of Reference Example 1 was repeated except that water was added in an amount of 40 ml (2%) and a compression molding pressure of 32 bar (kg/cm²) (force: 100 kg) was used to provide about 900 tablets.

Example 1

[0074] A granulating machine (Vertical Granulator VG10, Powrex) was charged with ascorbic acid, riboflavin butyrate, d- α -tocopherol, xylitol, maltitol, corn starch, aspartame and powdered acacia in the amounts indicated in Table 1 and the charge was mixed for 1 minute. Then, 32 ml of water was added and the mixture was kneaded. Using a single-punch tablet machine (Kikusui Seisakusho), the mixture was compression-molded with a flat punch having a beveled edge, 20 mm in diameter, at a molding pressure of 32 bar (kg/cm²) (force: 100 kg) to provide about 800 tablets. The tablets were dried in vacuo using a box type vacuum dryer (Kusuki Seisakusho).

Table 1

Formula	
Ingredient	Amount added (g)
Ascorbic acid	370
Sodium ascorbate	420
Riboflavin butyrate	2.2
d- α -Tocopherol	112

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Table 1 (continued)

Formula	
Ingredient	Amount added (g)
Xylitol	600
Maltitol	100
Corn starch	383.8
Aspartame	2
Powdered acacia	10
Total	2000

Example 2

[0075] A kneader (Universal Kneader, Hata Iron Works) was charged with diazepam, sucrose, glucose, potato starch, citric acid, gelatin and FD&C Yellow No. 6 in the amounts indicated in Table 2 and the charge was mixed for 2 minutes. Then, 10 ml of alcohol and 10 ml of water were added and the mixture was kneaded. Using a tablet machine (single-punch tablet machine, Kikusui Seisakusho), the mixture was compression-molded with a punch having a concave surface, 10 mm in diameter, at a molding pressure of 38 bar (kg/cm²) (force: 30 kg) to provide about 800 tablets. The tablets were dried in vacuo using a box type vacuum dryer (Kusuki Seisakusho).

Table 2

Formula	
Ingredient	Amount added (g)
Diazepam	1
Sucrose	271.45
Glucose	100
Potato starch	100
Citric acid	25
Gelatin	2.5
FD&C Yellow No. 6	0.05
Total	500

Example 3

[0076] A fluidized bed granulator (FD-5S, Powrex) was charged with ibuprofen, caffeine, erythritol, citric acid, carmellose calcium, corn starch, stevia and menthol in the amounts indicated in Table 3 and the charge was mixed for 3 minutes. The mixture was granulated while 20 ml of water was sprayed and the resulting granules were compression-molded with a flat punch having a rounded edge, 15 mm in diameter, at a molding pressure of 34 bar (kg/cm²) (force: 60 kg) to provide about 800 tablets. The tablets were air-dried in a mini-jet oven (Toyama Sangyo).

Table 3

Formula	
Ingredient	Amount added (g)
Ibuprofen	100
Caffeine	12.5
Erythritol	655.5
Citric acid	100
Carmellose calcium	30
Corn starch	100
Stevia	1
Menthol	1

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Table 3 (continued)

Formula	
Ingredient	Amount added (g)
Total	1000

Example 4

[0077] Except that the molding pressure was 10 bar (kg/cm²) (force: 30 kg), the procedure of Example 1 was otherwise repeated to provide about 800 tablets.

Example 5

[0078] Except that the kneading operation was carried out using 10 ml of water, the procedure of Example 1 was repeated to provide about 800 tablets.

Example 6

[0079] Except that the amount of water was 100 ml, the procedure of Example 1 was repeated to provide about 800 tablets.

Example 7

[0080] Except that the ingredients indicated in Table 4 and 36 ml of water were used, the procedure of Example 1 was repeated to provide about 800 tablets.

Table 4

Formula	
Ingredient	Amount added (g)
Ascorbic acid	303
Sodium L-ascorbate	409
Riboflavin butyrate	2
d- α -Tocopherol acetate	100
Pyridoxine hydrochloride	15
Xylitol	475
Sucrose	234
Maltitol	50
Potato starch	400
Powdered acacia	10
Aspartame	2
Total	2000

Example 8

[0081] Except that the ingredients indicated in Table 5 and 40 ml of water were used and the molding pressure was 36 bar (kg/cm²) (force: 110 kg), the procedure of Example 1 was repeated to provide about 800 tablets.

Table 5

Formula	
Ingredient	Amount added (g)
Acetaminophen	300
Ethenzamide	450

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Table 5 (continued)

Formula	
Ingredient	Amount added (g)
Anhydrous caffeine	50
Xylitol	405
Sucrose	233
Maltitol	50
Corn starch	500
Macrogol 6000	20
Powdered acacia	10
Aspartame	2
Total	2020

Example 9

[0082] Except that the ingredients indicated in Table 6 and 9 ml of water were used and the molding pressure was 101 bar (kg/cm²) (force: 80 kg), the procedure of Example 2 was repeated to provide about 1600 tablets.

Table 6

Formula	
Ingredient	Amount added (g)
Dimenhydrinate	50
Scopolamine hydrobromide	0.1
Caffeine	30
Sucrose	709.9
Corn starch	100
Potato starch	100
Powdered acacia	10
Total	1000

Example 10

[0083] Except that the ingredients indicated in Table 7 and 11 ml of water were used and the molding pressure was 127 bar (kg/cm²) (force: 100 kg), the procedure of Example 2 was repeated to provide about 1600 tablets.

Table 7

Formula	
Ingredient	Amount added (g)
Idebenone	30
Xylitol	500
Sucrose	215
Potato starch	250
Gelatin	5
Total	1000

Example 11

[0084] Except that the ingredients indicated in Table 8 and 28 ml of water were used and the molding pressure was 38 bar (kg/cm²) (force: 120 Kg), the procedure of Example 1 was repeated to provide about 800 tablets.

Table 8

Formula	
Ingredient	Amount added (g)
Acetaminophen	300
Chlorpheniramine maleate	2.5
Dihydrocodein phosphate	8
Noscapine	16
dl-Methylephedrine hydrochloride	20
Serratiopeptidase	5
Anhydrous caffeine	25
Kumulite®	90
Xylitol	800
Glucose	418.5
Corn starch	300
Powdered acacia	10
Aspartame	5
Total	2000

Example 12

[0085] Except that the ingredients indicated in Table 9 and 24 ml of water were used and the molding pressure was 35 bar (kg/cm²) (force: 110 Kg), the procedure of Example 1 was repeated to provide about 800 tablets.

Table 9

Formula	
Ingredient	Amount added (g)
Acetaminophen	300
Chlorpheniramine maleate	2.5
Dihydrocodein phosphate	8
Noscapine	16
dl-Methylephedrine hydrochloride	20
Serratiopeptidase	5
Guaifenesin	83
Ascorbic acid	100
Anhydrous caffeine	25
Sucrose	628
Erythritol	600
Potato starch	200
Powdered acacia	10
Saccharin sodium	2.5
Total	2000

Example 13

[0086] Except that the ingredients indicated in Table 10 and 20 ml of water were used and the molding pressure was 29 bar (kg/cm²) (force: 90 kg), the procedure of Example 1 was repeated to provide about 800 tablets.

Table 10

Formula	
Ingredient	Amount added (g)
Methocarbamol	500
Ethenzamide	300
Anhydrous caffeine	30
Tocopherol acetate	30
Dibenzoylthiamin	8
Maltitol	500
Xylitol	312
Corn starch	300
Gelatin	10
Menthol	5
Aspartame	5
Total	2000

Example 14

[0087] Except that the ingredients indicated in Table 11 and 24 ml of water were used, the procedure of Example 1 was repeated to provide about 800 tablets.

Table 11

Formula	
Ingredient	Amount added (g)
Tochu extracts	30
Ginseng extracts	100
Rokuzyo	5
Vitamin A	1×10^6 IU
Ascorbinic acid	125
d- α -Tocopherol acetate	5
Fursulthiamin hydrochloride	5
Riboflavin butyrate	5
Pyridoxine hydrochloride	12.5
Hydroxocobalamin acetate	30×10^{-3}
Dibasic calcium phosphate	20
Precipitated calcium carbonate	62
Sucrose	1305
Potato starch	300
Powdered acacia	10
Aspartame	10
Lemon oil	5
Total	2000

Example 15

[0088] Except that the ingredients indicated in Table 12 and 30 ml of water were used and the molding pressure was 30 bar (kg/cm²) (force: 90 Kg), the procedure of Example 1 was repeated to provide about 800 tablets.

Table 12

Formula	
Ingredient	Amount added (g)
Daiôkanzôtô extract powder	400
Xylitol	800
Sucrose	440
Potato starch	150
Corn starch	200
Powdered acacia	10
Total	2000

Example 16

[0089] Except that the ingredients indicated in Table 13 and 30 ml of water were used, the procedure of Example 1 was repeated to provide about 800 tablets.

Table 13

Formula	
Ingredient	Amount added (g)
Ascorbic acid	500
Sodium L-ascorbate	560
Riboflavin butyrate	3
Sucrose	512
Corn starch	400
Aspartame	5
Powdered acacia	15
Lemon oil	5
Total	2000

Example 17

[0090] Except that the ingredients indicated in Table 14 and 40 ml of water were used and the molding pressure was 29 bar (kg/cm²) (force: 90 kg), the procedure of Example 1 was repeated to provide about 800 tablets.

Table 14

Formula	
Ingredient	Amount added (g)
Kôshaheisankashakuyaku	700
Sucrose	985
Corn starch	300
Powdered acacia	10
Aspartame	5
Total	2000

Example 18

[0091] Except that the ingredients indicated in Table 15 and 24 ml of water were used and the molding pressure was 25 bar (kg/cm²) (force: 80 kg), the procedure of Example 1 was repeated to provide about 800 tablets.

Table 15

Formula	
Ingredient	Amount added (g)
Antyûsan	500
Sorbitol	700
Sucrose	485
Potato starch	300
Aspartame	5
Powdered acacia	10
Total	2000

Example 19

[0092] Except that the ingredients indicated in Table 16 and 10 ml of water were used and the molding pressure was 25 bar (kg/cm²) (force: 80 kg), the procedure of Example 1 was repeated to provide about 400 tablets.

Table 16

Formula	
Ingredient	Amount added (g)
Ipriflavon	200
Xylitol	645
Potato starch	150
Gelatin	5
Total	1000

Example 20

[0093] Except that the ingredients indicated in Table 17 and 16 ml of water were used, the procedure of Example 1 was repeated to provide about 800 tablets.

Table 17

Formula	
Ingredient	Amount added (g)
Methyldopa	500
Xylitol	800
Sucrose	280
Corn starch	400
Macrogol 6000	10
Powdered acacia	15
Aspartame	5
Total	2010

Example 21

[0094] Except that the ingredients indicated in Table 18 and 24 ml of water were used and the molding pressure was 25 bar (kg/cm²) (force: 80 kg), the procedure of Example 1 was repeated to provide about 800 tablets.

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Table 18

Formula	
Ingredient	Amount added (g)
Tolbutamide	500
Xylitol	1090
Potato starch	400
Powdered acacia	10
Total	2000

Example 22

[0095] Except that the ingredients indicated in Table 19 and 6 ml of alcohol and 6 ml of water were used and the mixture was compression-molded with a punch of 9 mm in diameter at a molding pressure of 31 bar (kg/cm²) (force: 20 Kg), the procedure of Example 2 was repeated to provide about 1000 tablets of 300 mg.

Table 19

Formula	
Ingredient	Amount added (g)
Diazepam	1
Xylitol	160
Sucrose	78
Potato starch	60
Powdered acacia	1
Total	300

Example 23

[0096] Except that the ingredients indicated in Table 20 were used, the procedure of Example 22 was repeated to provide about 1000 tablets of 300 mg.

Table 20

Formula	
Ingredient	Amount added (g)
Diazepam	10
Xylitol	160
Sucrose	68
Potato starch	60
Powdered acacia	1
Total	300

Example 24

[0097] Except that the ingredients indicated in Table 21 were used, the procedure of Example 22 was repeated to provide about 1000 tablets of 300 mg.

Table 21

Formula	
Ingredient	Amount added (g)
Diazepam	20

Table 21 (continued)

Formula	
Ingredient	Amount added (g)
Xylitol	160
Sucrose	58
Potato starch	60
Powdered acacia	1
Total	300

Test Examples

[0098] To illustrate the effects of the invention in further detail, the following characteristics of the tablets prepared in the foregoing Examples were determined. The results are shown in Table 22. Similar determinations were also made with the control tablets prepared in Reference Examples. The results are shown in Table 23.

(1) Porosity

[0099] The porosity of each tablet was determined using the following equation.

$$\text{Porosity} = \frac{\text{Volume of tablet} - \frac{\text{weight of tablet}}{\text{true density of ingredients}}}{\text{Volume of tablet}} \times 100$$

(2) Buccal solubility

[0100] The time to complete dissolution by saliva in the oral cavity was determined in a healthy adult male volunteer (45 years old, body height 165 cm, body weight 55 kg). The test was performed in duplicate and the mean of the results of two determinations was adopted.

(3) Disintegration time

[0101] The disintegration time of each tablet was determined in accordance with the disintegration test described in Japanese Pharmacopoeia XII. The mean of results of six determinations was adopted.

(4) Hardness

[0102] The hardness of each tablet was measured with a tablet hardness tester (TH-100, Toyama Sangyo). The test was performed in 10 runs and the mean of results of 10 determinations was adopted.

(5) Falling impact strength

[0103] Each tablet was dropped from a height of 30 cm on a glass plate and the degree of destruction was measured. The test was performed in 10 replicates and the mean result was adopted.

Table 22-1

	Example						
	1	2	3	4	5	6	7
Buccal dissolution time (min)	0.8	0.5	0.6	0.3	0.5	1.2	1.2
Disintegration time (min)	0.5	0.4	0.3	0.2	0.4	0.8	0.6
Hardness (kg)	14	5	7	7	10	16	12
Falling impact strength (%)	0	0	0	60	50	0	0
Porosity (%)	45	53	38	65	50	39	46
Molding pressure (kg/cm ²)	32	38	34	10	32	32	32
Water used (% (w/w))	1.6	2.0	2.0	1.6	0.5	5.0	1.8

Table 22-2

	Example						
	8	9	10	11	12	13	14
Buccal dissolution time (min.)	1.0	0.8	0.8	1.4	1.2	1.1	1.5
Disintegration time (min.)	0.5	0.4	0.5	0.8	0.8	0.7	0.8
Hardness (kg)	10	10	10	14	12	8	13
Falling impact strength (%)	0	0	0	0	0	0	0
Porosity (%)	36	52	50	30	32	35	39
Molding pressure (kg/cm ²)	36	101	127	38	35	29	32
Water used (% (w/w))	2.0	0.9	1.1	1.4	1.2	1.0	1.2

Table 22-3

	Example						
	15	16	17	18	19	20	21
Buccal dissolution time (min)	1.0	1.2	1.3	1.0	0.7	0.8	0.8
Disintegration time (min)	0.6	0.6	0.9	0.7	0.4	0.6	0.6
Hardness (kg)	10	12	14	10	8	12	10
Falling impact strength (%)	0	0	0	0	0	0	0
Porosity (%)	40	38	41	45	55	49	60
Molding pressure (kg/cm ²)	30	32	29	25	25	32	25
Water used (% (w/w))	1.5	1.5	2.0	1.2	1.0	0.8	1.2

Table 23

	Reference Example			
	1	2	3	4
Buccal dissolution time (min)	12	8	12	2.5
Disintegration time (min)	10	6	7	2.1

Table 23 (continued)

	Reference Example			
	1	2	3	4
Hardness (kg)	19	8	11	8
Falling impact strength (%)	90	50	90	80
Porosity (%)	15	13	17	40
Molding pressure (kg/cm ²)	1910	1980	1700	32
Water used (% (w/w))	10	10	12	2

[0104] Comparison of Tables 22 and 23 indicate that the fast dissolving tablet of the present invention is superior in solubility and disintegrability and yet has an adequate mechanical strength.

Claims

1. A fast dissolving or disintegrating tablet which comprises an effective amount of an active ingredient and a carbohydrate component, wherein said carbohydrate component comprises at least erythritol, and which has a porous structure with a hardness of 2 to 25 kg as determined with the tablet hardness tester TH-100 from Toyama Sangyo and a porosity of 20 to 80% as determined according to the following equation:

$$\text{Porosity} = \frac{\text{Vol. of tablet} - (\text{wt. of tablet} / \text{true density of ingredients})}{\text{Vol. of tablet}} \times 100.$$

2. The tablet according to claim 1 which contains 0.05 to 90% by weight of active ingredient and which has a falling impact strength of 0 to 70% which is the degree of destruction when the tablet is dropped from the height of 30 cm on a glass plate.
3. The tablet according to claim 2 wherein the particles of said carbohydrate component are adhered by drying the compression-molded tablet comprising the moistened particles of the carbohydrate component at their surface.
4. The tablet according to claim 2 which has a hardness of 3 to 20 kg, a porosity of 30 to 70% and a falling impact strength of 0 to 40%.
5. The tablet according to claim 2 which contains 10 to 90% by weight of said carbohydrate component.
6. The tablet according to claim 2 which has a disintegration time of 0.05 to 3.0 minutes and a buccal solubility of 0.05 to 3.0 minutes.
7. A fast dissolving or disintegrating tablet obtainable by a method which comprises
 - (a) wetting a mixture comprising an active ingredient and a carbohydrate component with 0.3 to 10% by weight of water, based on the weight of a composition comprising said active ingredient, said carbohydrate and water, to moisten the surface of particles of said carbohydrate component, wherein said carbohydrate component comprises at least erythritol;
 - (b) compression molding said composition into a fast dissolving or disintegrating tablet form; and
 - (c) drying said tablet.
8. The tablet according to claim 7 wherein said surface of particles of said carbohydrate component are adhered by compression-molding said composition comprising the moistened particles of the carbohydrate component at their surface and drying the compression-molded tablet.
9. The tablet according to claim 7 which has a porous structure with a porosity of 20 to 80% as determined according to the following equation:

$$\text{Porosity} = \frac{\text{Vol. of tablet} - (\text{wt. of tablet} / \text{true density of ingredients})}{\text{Vol. of tablet}} \times 100.$$

- 5 10. The tablet according to claim 9 which has a hardness of 2 to 25 kg as determined with the tablet hardness tester TH-100 from Toyama Sangyo.
11. The tablet according to claim 1 or 10 which has a porous structure with a porosity of 30 to 70%, a hardness of 3 to 20 kg, and a disintegration time of 0.05 to 3.0 minutes.
- 10 12. The tablet according to claim 11 which further has a falling impact strength of 0 to 70% which is the degree of destruction when the tablet is dropped from the height of 30 cm on a glass plate and buccal solubility of 0.05 to 3.0 minutes.
- 15 13. The tablet according to claim 1 or 7 which contains 0.05 to 90% by weight of said active ingredient and 10 to 90% by weight of said carbohydrate component.
- 20 14. The tablet according to claim 1, 2 or 7 which contains at least one member selected from a vitamin, a crude drug, an antipyretic-analgesic-antiinflammatory agent, an antipsychotic drug, an antianxiety drug, an antidepressant, a hypnotic-sedative agent, a gastrointestinal function conditioning agent, an antitussive-expectorant, an antihypertensive drug, an antacid, an antidiabetic agent, a drug for osteoporosis or a skeletal muscle relaxant as said active ingredient.
- 25 15. The tablet according to any of claims 1 or 7 to 10 which contains 0.05 to 90% by weight of said active ingredient, 10 to 90% by weight of said carbohydrate component and has a porous structure with a porosity of 20 to 80%.
- 30 16. The tablet according to claim 15 which contains 0.1 to 10% by weight of said active ingredient and 50 to 85% by weight of said carbohydrate component.
17. The tablet according to claim 15 which contains 10 to 30% by weight of said active ingredient and 30 to 80% by weight of said carbohydrate component.
- 35 18. The tablet according to claim 16 which contains 30 to 70% by weight of said active ingredient and 10 to 70% by weight of said carbohydrate component.
19. The tablet according to claim 1 or 10 which has a hardness of 3 to 20 kg and a porosity of 30 to 70%.
20. The tablet according to claim 7 wherein said water is removed.
- 40 21. Use of erythritol for producing a fast dissolving or disintegrating tablet comprising an active ingredient and erythritol as a carbohydrate component.

Patentansprüche

- 45 1. Sich schnell auflösende oder schnell zerfallende Tablette, die eine wirksame Menge eines Wirkstoffs und eine Kohlenhydratkomponente umfasst, wobei die Kohlenhydratkomponente wenigstens Erythrit umfasst, wobei die Tablette eine poröse Struktur mit einer mit dem Tablettenhärte tester TH-100 von Toyama Sangyo bestimmten Härte von 2 bis 25 kg und einer gemäß der folgenden Gleichung berechneten Porosität von 20 bis 80% hat:

$$50 \quad \text{Porosität} = \frac{\text{Vol. der Tablette} - (\text{Gew. der Tablette} / \text{wahre Dichte der Bestandteile})}{\text{Volumen der Tablette}} \times 100.$$

2. Tablette gemäß Anspruch 1, die 0,05 bis 90 Gew.-% Wirkstoff enthält und eine Falltest-Stoßfestigkeit von 0 bis 70% hat, welche dem Grad der Zerstörung entspricht, wenn man die Tablette aus einer Höhe von 30 cm auf eine Glasplatte fallen lässt.
- 55 3. Tablette gemäß Anspruch 2, wobei die Teilchen der Kohlenhydratkomponente festgeheftet werden, indem man die formgepresste Tablette, die die angefeuchteten Teilchen der Kohlenhydratkomponente an deren Oberfläche

umfasst, trocknet.

4. Tablette gemäß Anspruch 2, die eine Härte von 3 bis 20 kg, eine Porosität von 30 bis 70% und eine Falltest-Stoßfestigkeit von 0 bis 40% hat.

5. Tablette gemäß Anspruch 2, die 10 bis 90 Gew.-% der Kohlenhydratkomponente enthält.

6. Tablette gemäß Anspruch 2, die eine Zerfallszeit von 0,05 bis 3,0 Minuten und eine bukkale Löslichkeit von 0,05 bis 3,0 Minuten hat.

7. Sich schnell auflösende oder schnell zerfallende Tablette, die nach einem Verfahren erhältlich ist, das folgendes umfasst:

(a) Benetzen eines Gemischs, das einen Wirkstoff und eine Kohlenhydratkomponente umfasst, mit 0,3 bis 10 Gew.-% Wasser, bezogen auf das Gewicht einer Zusammensetzung, die den Wirkstoff, das Kohlenhydrat und Wasser umfasst, so dass die Oberfläche von Teilchen der Kohlenhydratkomponente angefeuchtet wird, wobei die Kohlenhydratkomponente wenigstens Erythrit umfasst;

(b) Formpressen der Zusammensetzung in die Form einer sich schnell auflösenden oder schnell zerfallenden Tablette; und

(c) Trocknen der Tablette.

8. Tablette gemäß Anspruch 7, wobei die Oberflächen von Teilchen der Kohlenhydratkomponente festgeheftet werden, indem man die Zusammensetzung, die die angefeuchteten Teilchen der Kohlenhydratkomponente an deren Oberfläche umfasst, formpresst und die formgepresste Tablette trocknet.

9. Tablette gemäß Anspruch 7, die eine poröse Struktur mit einer gemäß der folgenden Gleichung berechneten Porosität von 20 bis 80% hat:

$$\text{Porosität} = \frac{\text{Vol. der Tablette} - (\text{Gew. der Tablette} / \text{wahre Dichte der Bestandteile})}{\text{Volumen der Tablette}} \times 100.$$

10. Tablette gemäß Anspruch 9, die eine mit dem Tablettenhärteprüfer TH-100 von Toyama Sangyo bestimmte Härte von 2 bis 25 kg hat.

11. Tablette gemäß Anspruch 1 oder 10, die eine poröse Struktur mit einer Porosität von 30 bis 70%, einer Härte von 3 bis 20 kg und einer Zerfallszeit von 0,05 bis 3,0 Minuten hat.

12. Tablette gemäß Anspruch 11, die weiterhin eine Falltest-Stoßfestigkeit von 0 bis 70%, welche dem Grad der Zerstörung entspricht, wenn man die Tablette aus einer Höhe von 30 cm auf eine Glasplatte fallen lässt, und eine bukkale Löslichkeit von 0,05 bis 3,0 Minuten hat.

13. Tablette gemäß Anspruch 1 oder 7, die 0,05 bis 90 Gew.-% des Wirkstoffs und 10 bis 90 Gew.-% der Kohlenhydratkomponente enthält.

14. Tablette gemäß Anspruch 1, 2 oder 7, die als Wirkstoff wenigstens einen Vertreter enthält, der ausgewählt ist aus einem Vitamin, einer Rohdroge, einem antipyretischen-analgetischen-entzündungshemmenden Mittel, einem antipsychotischen Wirkstoff, einem angstlösenden Wirkstoff, einem Antidepressivum, einem Hypnotikum-Sedativum, einem Konditionierungsmittel der Magen-Darm-Funktion, einem Antitussivum-Expektorans, einem Antihypertonikum, einem Antacidum, einem Antidiabetikum, einem Wirkstoff gegen Osteoporose oder einem Skelettmuskelrelaxans.

15. Tablette gemäß einem der Ansprüche 1 oder 7 bis 10, die 0,05 bis 90 Gew.-% des Wirkstoffs und 10 bis 90 Gew.-% der Kohlenhydratkomponente enthält und eine poröse Struktur mit einer Porosität von 20 bis 80% hat.

16. Tablette gemäß Anspruch 15, die 0,1 bis 10 Gew.-% des Wirkstoffs und 50 bis 85 Gew.-% der Kohlenhydratkomponente enthält.

17. Tablette gemäß Anspruch 15, die 10 bis 30 Gew.-% des Wirkstoffs und 30 bis 80 Gew.-% der Kohlenhydratkomponente enthält.
18. Tablette gemäß Anspruch 16, die 30 bis 70 Gew.-% des Wirkstoffs und 10 bis 70 Gew.-% der Kohlenhydratkomponente enthält.
19. Tablette gemäß Anspruch 1 oder 10, die eine Härte von 3 bis 20 kg und eine Porosität von 30 bis 70% hat.
20. Tablette gemäß Anspruch 7, wobei das Wasser entfernt wird.
21. Verwendung von Erythrit zur Herstellung einer sich schnell auflösenden oder schnell zerfallenden Tablette, die einen Wirkstoff und Erythrit als Kohlenhydratkomponente umfasst.

Revendications

1. Comprimé à dissolution et à délitement rapide, comprenant une quantité efficace d'un principe actif et d'un hydrate de carbone, dans lequel ledit hydrate de carbone comprend au moins de l'érythritol, et qui a une structure poreuse avec une dureté, mesurée à l'aide de l'appareil de mesure de la dureté de comprimés TH-100 de la société Toyama Sangyo, comprise entre 2 et 25 kg, et une porosité comprise entre 20 et 80 %, déterminée à l'aide de l'équation suivante :

$$\text{porosité} = \frac{\text{vol. comprimé} - (\text{poids du comprimé} / \text{vraie masse volumique des ingrédients})}{\text{volume du comprimé}}$$

2. Comprimé selon la revendication 1, contenant de 0,05 à 90 % en poids d'un principe actif et qui a une résistance au choc par chute comprise entre 0 et 70 %, cette valeur correspondant au degré de destruction lorsqu'on laisse le comprimé tomber d'une hauteur de 30 cm sur une plaque en verre.
3. Comprimé selon la revendication 2, dans lequel les particules dudit hydrate de carbone sont collées par séchage du comprimé moulé sous pression comprenant des particules d'hydrate de carbone mouillées en surface.
4. Comprimé selon la revendication 2, qui a une dureté comprise entre 3 et 20 kg, une porosité comprise entre 30 et 70 % et une résistance au choc par chute comprise entre 0 et 40 %.
5. Comprimé selon la revendication 2, qui contient de 10 à 90 % en poids dudit hydrate de carbone.
6. Comprimé selon la revendication 2, qui a une durée de délitement comprise entre 0,05 et 3,0 minutes et un temps de solubilisation dans la bouche comprise entre 0,05 et 3,0 minutes.
7. Comprimé à dissolution et délitement rapide que l'on peut obtenir selon le procédé comprenant les étapes consistant
 - (a) à mouiller un mélange comprenant un principe actif et un hydrate de carbone avec de 0,3 à 10 % en poids d'eau, rapporté au poids d'une composition contenant ledit principe actif, ledit hydrate de carbone et l'eau, afin de mouiller la surface des particules dudit hydrate de carbone, ledit hydrate de carbone comprenant au moins de l'érythritol,
 - (b) à mouler ladite composition sous pression de manière à obtenir un comprimé à dissolution et délitement rapide, et
 - (c) à sécher ledit comprimé.
8. Comprimé selon la revendication 7, dans lequel les particules dudit hydrate de carbone sont collées au niveau de leur surface par moulage sous pression de ladite composition comprenant les particules d'hydrate de carbone mouillées en surface, et séchage du comprimé moulé sous pression.
9. Comprimé selon la revendication 7, qui a une structure poreuse avec une porosité comprise entre 20 et 80 %, déterminée à l'aide de l'équation suivante :

$$\text{porosité} = \frac{\text{vol. comprimé} - (\text{poids du comprimé/vraie masse volumique des ingrédients})}{\text{volume du comprimé}}$$

- 5 10. Comprimé selon la revendication 9, ayant une dureté, mesurée à l'aide de l'appareil de mesure de la dureté de comprimés TH-100 de la société Toyama Sangyo, comprise entre 2 et 25 kg.
11. Comprimé selon la revendication 1 ou 10, qui a une structure poreuse avec une porosité comprise entre 30 et 70 %, une dureté comprise entre 3 et 20 kg et un temps de délitement compris entre 0,05 et 3,0 minutes.
- 10 12. Comprimé selon la revendication 11, qui présente en outre une résistance au choc par chute comprise entre 0 et 70 %, qui correspond au degré de destruction lorsqu'on laisse le comprimé tomber d'une hauteur de 30 cm sur une plaque en verre, et un temps de dissolution dans la bouche compris entre 0,05 et 3,0 minutes.
- 15 13. Comprimé selon la revendication 1 ou 7, contenant de 0,05 à 90 % en poids dudit principe actif et de 10 à 90 % en poids dudit hydrate de carbone.
- 20 14. Comprimé selon la revendication 1, 2 ou 7, qui contient, en tant que principe actif, au moins un élément choisi dans le groupe formé par une vitamine, un principe actif brut, un agent antipyrétique-analgésique-anti-inflammatoire, un agent antipsychotique, un agent anxiolytique, un agent anti-dépresseur, un agent hypnotique-sédatif, un agent de conditionnement de la fonction gastro-intestinale, un agent expectorant-anti-toussif, un agent anti-hypertenseur, un anti-acide, un agent anti-diabétique, un principe actif contre l'ostéoporose ou un agent relaxateur des muscles.
- 25 15. Comprimé selon l'une quelconque des revendications 1 ou 7 à 10, contenant de 0,05 à 90 % en poids dudit principe actif et de 10 à 90 % en poids dudit hydrate de carbone, et ayant une structure poreuse avec une porosité comprise entre 20 % et 80 %.
- 30 16. Comprimé selon la revendication 15, contenant de 0,1 à 10 % en poids dudit principe actif et de 50 à 85 % en poids dudit hydrate de carbone.
- 35 17. Comprimé selon la revendication 15 contenant de 10 à 30 % en poids dudit principe actif et de 30 à 80 % en poids dudit hydrate de carbone.
18. Comprimé selon la revendication 16, contenant de 30 à 70 % en poids dudit principe actif et de 10 à 70 % en poids dudit hydrate de carbone.
19. Comprimé selon la revendication 1 ou 10, qui a une dureté comprise entre 3 et 20 kg et une porosité comprise entre 30 et 70 %.
- 40 20. Comprimé selon la revendication 7, dont ladite eau est éliminée.
21. Utilisation d'érythritol pour la préparation d'un comprimé à dissolution et délitement rapide comprenant un principe actif et de l'érythritol en tant qu'hydrate de carbone.

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